

This listing of claims will replace all prior versions, and listings of claims in the application.

**In the Claims:**

1. (Currently amended) A method for increasing JNK activation leading to programmed cell death, said method comprising:
  - (a) selecting a peptide comprising an amino acid sequence within the kinase domain of JNKK2 ~~an agent~~ that blocks suppression of JNK activation by Gadd45 $\beta$ ; and
  - (b) ~~using~~ contacting a cell with the ~~agent~~ peptide to increase programmed cell death due to the activation of JNKK2.
2. (Cancelled)
3. (Withdrawn) The method of claim 2, wherein the agent is an antisense molecule to a *gadd45 $\beta$*  gene sequence or fragments thereof.
4. (Withdrawn) The method of claim 2, wherein the agent is a small interfering RNA molecule (siRNA).
5. (Withdrawn) The method of claim 2, wherein the agent is a ribozyme molecule.
6. (Currently amended) The method of claim 1, wherein the ~~agent~~ peptide is a cell-permeable peptide.
7. (Withdrawn) The method of claim 2, wherein the agent is a small molecule.
8. (Withdrawn) The method of claim 6, wherein the molecule is a peptide mimetic that mimics the functions of a Gadd45 protein.
9. (Withdrawn) The method of claim 1, said method comprising:
  - (a) interfering with the target by obtaining a molecule that suppresses JNK signaling by interacting with a Gadd45-binding region on JNKK2; and
  - (b) contacting a cell with the molecule to protect the cell from programmed cell death.
10. (Withdrawn) The method of claim 9, comprising:
  - (a) obtaining a cDNA molecule that encodes a full length or portions of a Gadd45 protein;
  - (b) transfecting the cell with the cDNA molecule; and
  - (c) providing conditions for expression of the cDNA in the cell so that JNKK2 is bound and unavailable to activate the JNK pathway that induces programmed cell death.

11. (Withdrawn) The method of claim 10, wherein the cDNA molecule encodes a fragment of Gadd45 protein that is sufficient to suppress JNK signaling.
12. (Withdrawn) The method of claim 10, wherein the cDNA molecule encodes a peptide that corresponds to amino acids 69-113 of Gadd45 $\beta$ .
13. (Withdrawn) The method of claim 10, wherein the programmed cell death is induced by TNF $\alpha$ .
14. (Withdrawn) The method of claim 10, wherein the programmed cell death is induced by Fas.
15. (Withdrawn) The method of claim 10, wherein the programmed cell death is induced by TRAIL.
16. (Withdrawn) The method of claim 10, wherein the programmed cell death is induced by a genotoxic agent.
17. (Withdrawn) The method of claim 16, wherein the agent is selected from the group consisting of daunorubicin and cisplatin.
18. (Withdrawn) A method to identify agents that modulate JNK signaling, said method comprising:
  - (a) determining whether the agent binds to Gadd45 $\beta$ ; and
  - (b) assaying for activity of the bound Gadd45 $\beta$  to determine the effect on JNK signaling.
19. (Withdrawn) A method for obtaining a mimetic that is sufficient to suppress JNK activation by interacting with JNKK2, said method comprising:
  - (a) designing the mimetic to mimic the function of a Gadd45 protein;
  - (b) contacting the mimetic to a system that comprises the JNK pathway; and
  - (c) determining whether there is suppression of JNK signaling.
20. (Withdrawn) A method for screening and identifying an agent that modulates JNK pathway *in vitro*, said method comprising:
  - (a) obtaining a target component of the JNK pathway;
  - (b) exposing a cell to the agent; and
  - (c) determining the ability of the agent to modulate the JNK pathway.
21. (Withdrawn) The agent in claim 20, is selected from a group consisting of peptides,

peptide mimetics, peptide-like molecules, mutant proteins, cDNAs, antisense oligonucleotides or constructs, lipids, carbohydrates, and synthetic or natural chemical compounds.

- 22.** (Withdrawn) A method for screening and identifying an agent that modulates JNK activity *in vivo*, said method comprising:
- (a) obtaining a candidate agent;
  - (b) administering the agent to a non-human animal; and
  - (c) determining the level of JNK activity in the animal compared to JNK activity in animals not receiving the agent.
- 23.** (Withdrawn) A method for identifying an agent that prevents Gadd45 $\beta$  from blocking apoptosis, said method comprising:
- (a) contacting cells that express high levels of Gadd45 $\beta$  which are protected against TNF $\alpha$ -induced apoptosis with the agent and TNF $\alpha$ ;
  - (b) comparing apoptosis in the cells in (a) with control cells exposed to the agent but not to TNF $\alpha$ ; and
  - (c) inferring from differences in apoptosis in treated versus control cells, whether the agent prevents Gadd45 $\beta$  from blocking apoptosis.
- 24.** (Withdrawn) A method for screening for a modulator of the JNK pathway, said method comprising:
- (a) obtaining a candidate modulator of the JNK pathway, wherein the candidate is potentially any agent capable of modulating a component of the JNK pathway, including peptides, mutant proteins, cDNAs, anti-sense oligonucleotides or constructs, synthetic or natural chemical compounds;
  - (b) administering the candidate agent to a cancer cell;
  - (c) determining the ability of the candidate substance to modulate the JNK pathway, including either upregulation or downregulation of the JNK pathway and assaying the levels of up or down regulation.
- 25.** (Withdrawn) A method of treating degenerative disorders and other conditions caused by effects of apoptosis in affected cells, said method comprising:
- (a) obtaining a molecule that interferes with the activation of JNK pathways; and
  - (b) contacting the affected cells with the molecule.

- 26.** (Withdrawn) A method of aiding the immune system to kill cancer cells by augmenting JNK signaling, said method comprising:
- (a) obtaining an inhibitor to block JNK signaling; and
  - (b) contacting the cancer cells with the inhibitor.
- 27.** (Withdrawn) The method of claim 26, wherein the inhibitor blocks activation of JNKK2 by Gadd45 $\beta$ .
- 28.** (Withdrawn) A method for transactivating a *gadd45 $\beta$*  promoter, said method comprising:
- (a) binding NF- $\kappa$ B complexes to promoter elements of *gadd45 $\beta$* ; and
  - (b) assaying for *gadd45 $\beta$*  gene expression.
- 29.** (Withdrawn) A method for treating cancer, said method comprising:
- (a) increasing JNK activity by inhibiting Gadd45 $\beta$  function; and
  - (b) administering inhibitors that interfere with Gadd45 $\beta$  function.
- 30.** (Withdrawn) A method to determine agents that interfere with binding between Gadd45 protein and JNKK2, said method comprising:
- (a) obtaining an agent that binds to Gadd45 protein;
  - (b) contacting a cell with the agent under conditions that would induce transient JNK activation; and
  - (c) comparing cells contacted with the agent to cells not contacted with the agent to determine if the JNK pathway is activated.
- 31.** (Withdrawn) A molecule with a nucleotide sequence having Gene Bank Acc. # AF441860 that functions as a *gadd45 $\beta$*  promoter.
- 32.** (Withdrawn) A molecule with a nucleotide sequence that is an element of the promoter at amino acid positions selected from the group consisting of positions -447/-438 ( $\kappa\beta$ -1), -426/-417 ( $\kappa\beta$ -2), -377/-368 ( $\kappa\beta$ -3) according to FIG. 8.
- 33.** (Withdrawn) A molecule comprising a region of Gadd45 $\beta$ , characterized by the amino acid sequence from positions 60-114 of the full length of Gadd45 $\beta$  protein.
- 34.** (Withdrawn) A molecule comprising a binding region of JNKK2 characterized by the amino acid sequence from positions 132-156 of SEQ ID NO: 50 (GPVWKMRFRKTGHVIAVKQMRRSGN) of the full length JNKK2.

- 35.** (Withdrawn) A molecule comprising a binding region of JNKK2 characterized by the amino acid sequence from positions 220-234 of SEQ ID NO: 50 (GKMTVAIVKALYYLK) of the full length JNKK2.
- 36.** (Previously presented) The method of claim 6, wherein the peptide comprises the amino acid sequence from positions 132-156 of SEQ ID NO: 50, wherein the sequence is GPVWKMRFRKTGHVIAVKQMRRSGN.
- 37.** (Withdrawn) The method of claim 6, wherein the peptide comprises the amino acid sequence from positions 220-234 of SEQ ID NO: 50, wherein the sequence is GKMTVAIVKALYYLK.